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EXAMINER	
DUFFY, BRADLEY	

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1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,791	REES ET AL.	
	Examiner	Art Unit	
	BRADLEY DUFFY	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 13-31* is/are pending in the application.

4a) Of the above claim(s) *1-6,10,13-25,29 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-9,26-28 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/29/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Exhibits A and B*.

DETAILED ACTION

1. The election with traverse filed March 12, 2008, is acknowledged and has been entered.

Applicant has elected the invention of Group II, claims 7-9, 26, 27, 28 and 31[1], drawn to isolated proteins comprising an amino acid sequence encoded by: a) a nucleic acid encoding SEQ ID NO: 1, a nucleic acid that encodes a polypeptide at least 80% identical to SEQ ID NO:1, or a fragment thereof, b) nucleic acid molecules comprising the nucleotide sequence depicted between nucleic acid residues 642 and 1688 of SEQ ID NO: 2, c) nucleic acid molecules which specifically hybridizes to said nucleic acid molecules, d) nucleic acid molecules the sequence of which differs from the sequence of said nucleic acid molecules due to the degeneracy of the genetic code, derivatives or fragments of said proteins and kits and immunogenic compositions comprising said proteins.

2. Claims 1-10 and 13-31 are pending in the application.

3. Claims 1-6, 10, 13-25, 29 and 30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed March 12, 2008.

4. Claims 7-9, 26-28 and 31 are under examination.

[1] Claim 26 was inadvertently placed in Group I in the restriction requirement mailed 12/12/2007. Since claim 26 recites a vaccine comprising the protein according to claim 7, this claim is clearly drawn to the invention of Group II. The Examiner apologizes for any inconvenience this oversight may have caused Applicant or Applicant's representative.

Election/Restrictions

5. Applicant's traversal of the restriction and election requirement set forth in the Office action mailed December 12, 2007, is acknowledged.

Applicant's arguments have been carefully considered but have not been found persuasive for the following reasons:

At pages 6 and 7 of the response filed March 12, 2008, Applicant appears to be traversing the restriction requirement on the grounds that that the prior art disclosure by Lisziewicz et al. of a mixture of nucleic acids that comprise nucleic acids that specifically hybridize with a nucleic acid molecule encoding SEQ ID NO:1 would not fairly be characterized as being isolated.

In response this argument is not found persuasive, because e.g., before the mixture of nucleic acids of Lisziewicz et al. was used in an experiment, it would be considered isolated, i.e., separated from the other components used in such an experiment. In this case, it is apparent that the claimed nucleic acid molecules need not be the only nucleic acid molecule in the mixture because claim 1 recites that the nucleic acid molecules are selected from “nucleic acid molecules" a, b c or d. Consequently, it is apparent that the term “isolated” would not distinguish the nucleic acid molecules recited in claim 1 from the nucleic acid molecules recited in Lisziewicz et al for the reasons set forth in the restriction requirement mailed December 12, 2007. Furthermore, it is noted that PCT Rules 13.1 and 13.2 do not provide for a single general inventive concept to comprise more than the first mentioned product, the first mentioned method for making said product, and the first mentioned method for using said product.

Therefore, for these reasons, the restriction/election requirement is deemed proper and therefore made FINAL.

Information Disclosure Statement

6. The references cited in the information disclosure statement filed September 29, 2006, have been considered.

Specification

7. The disclosure is objected to for the following reasons:

(a) The disclosure is objected to because the disclosure refers to embedded hyperlinks and/or other forms of browser-executable code and to the Internet contents so identified. Reference to hyperlinks and/or other forms of browser-executable code and to the Internet contents so identified is impermissible and therefore requires deletion.

Examples of such impermissible disclosures appear in the specification at, for example, paragraph pages 18 and 19.

The attempt to incorporate essential or non-essential subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP § 608.01(p), paragraph I regarding acceptable incorporation by reference. See 37 CFR § 1.57.

MPEP 608.01(p) does not provide for incorporation of essential *or* non-essential material by reference to, for example, hyperlinks or other forms of browser-executable code. Essential subject matter may only be incorporated by reference to (1) US patents and pending US applications, or patents or other publications published by a foreign country or a regional patent office, (2) non-patent publications, (3) a US patent or application which itself incorporates material by reference, or (4) a foreign application. Non-essential information may be incorporated by reference to (1) patents or applications published by the United States, or patents or other publications published by a foreign country or a regional patent office, (2) prior filed, commonly owned US applications, (3) non-patent publications.

(b) The specification is objected to because the use of improperly demarcated trademarks has been noted in this application. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

Examples of such improperly demarcated trademarks appearing in the specification are GenBank® (see e.g., page 2) and Mx4000® (see e.g., page 18). Appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at <http://www.uspto.gov/web/menu/search.html>.

(c) The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Appropriate correction is required.

Claim Objections

8. Claims 7-9, 27, 28 and 31 are objected to because of the following informalities: Claim 7 refers to non-elected claim 1 which has accordingly been withdrawn from further consideration. Appropriate correction is required (i.e., claim 7 should be rewritten in independent form).

9. Claim 4, although not drawn to the elected invention, is objected to because it has been misnumbered as claim 14.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 7-9, 26, 27, 28 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 7-9, 26, 27, 28 and 31 are indefinite for being drawn to polypeptides encoded by "nucleic acid molecules, the complementary strand of which *specifically hybridises* to a nucleic acid molecule" in claim 7. At page 5, the specification discloses that: [t]he term "specifically hybridising" is intended to mean that the nucleic acid molecule can hybridise to nucleic acid molecules according to the invention under conditions of high stringency. Typical conditions for high stringency include 0.1 x SET, 0.1% SDS at 68°C for 20 minutes. Accordingly, since the specification does not provide a limiting definition of stringent conditions, it is submitted that the specification does not provide a standard for ascertaining the requisite degree of stringency that must be used to unambiguously determine which nucleic acid molecules specifically hybridize and which do not. In this case, the stringent hybridization conditions used in identifying such nucleic acids can vary, such that those conditions would allow different oligonucleotides to hybridize or not depending on the conditions used. Therefore, the metes and bounds of the subject matter that Applicant regards as the invention will vary; accordingly, these claims fail to delineate the metes and bounds of the subject matter that Applicant regards as the invention with the requisite particularity and clarity.

b. Claims 26, 27, 28 and 31 are indefinite for reciting "a pharmaceutically effective fragment" in these claims. The metes and bounds of the subject matter that Applicant regards as the invention cannot be ascertained, where the claims recite the phrase "pharmaceutically effective", yet fail to state the function that is necessarily achieved. In this case, it is unclear what function the fragment is required to have to be "pharmaceutically effective". Polypeptides are expected to have multiple different effects and it is unclear to which function the claim is directed. Which of the expected plurality of biological activities of the claimed polypeptides must be retained by the fragment for it to be "pharmaceutically effective"? The claims cannot be construed unambiguously without knowing the answer to this question. Thus, the claim fails to

delineate the subject matter that Applicant regards as the invention with the requisite degree of clarity and particularity to permit the skilled artisan to know or determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

Accordingly, these claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 7-9, 26-28 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "written description" rejection.

The considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, ``Written Description'' Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001; hereinafter "Guidelines"). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

These guidelines state that rejection of a claim for lack of written description, where the claim recites the language of an original claim should be rare. Nevertheless, these guidelines further state, "the issue of a lack of written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the

applicant has possession of the claimed invention" (*Id.* at 1105). The "Guidelines" continue:

> The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art. This problem may arise where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process.

Furthermore, the Federal Circuit has commented that each case involving the issue of written description, "must be decided on its own facts. Thus, the precedential value of cases in this area is extremely limited." *Vas-Cath*, 935 F.2d at 1562 (quoting *In re Driscoll*, 562 F.2d 1245, 1250 (C.C.P.A. 1977)). See *Noelle v. Lederman*, 69 USPQ2d 1508 (CAFC 2004).

Finally, with further regard to the proposition that, as *original* claims, the claims themselves provide *in haec verba* support themselves provide *in haec verba* support sufficient to satisfy the written description requirement, the Federal Circuit has explained that *in ipsis verbis* support for the claims in the specification does not *per se* establish compliance with the written description requirement:

> Even if a claim is supported by the specification, the language of the specification, to the extent possible, must describe the claimed invention so that one skilled in the art can recognize what is claimed. The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). *See also:* University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 1892 (CA FC 2004).

Thus, an original claim may provide written description for itself, but it must still be an adequate written description, *which establishes that the inventor was in possession of the invention*.

In the instant case, the claims are broadly drawn to a structurally and functionally diverse genus of "proteins comprising **an** amino acid sequence encoded by: a) a nucleic acid encoding SEQ ID NO: 1, a nucleic acid that encodes a polypeptide at least 80% identical to SEQ ID NO:1, or a fragment thereof, which is capable of cross-reacting with sera from patients with prostate cancer, b) nucleic acid molecules comprising the nucleotide sequence depicted between nucleic acid residues 642 and 1688 of SEQ ID NO: 2, c) nucleic acid molecules which specifically hybridizes to said nucleic acid molecules, d) nucleic acid molecules the sequence of which differs from the sequence of said nucleic acid molecules due to the degeneracy of the genetic code, derivatives or fragments of said proteins". Claim 8 is further drawn to a structurally and functionally diverse genus of proteins according to claim 7 comprising the amino acid sequence of SEQ ID NO:1.

In this case, as will be explained in further detail below, because one of ordinary skill in the art could not immediately envision, recognize or predict the structure and/or function of the genus of "proteins comprising **an** amino acid sequence" encoded by the recited nucleic acids sequences, derivatives or fragments of said proteins or the structure and/or function of the genus of "proteins comprising the amino acid sequence of SEQ ID NO:1", the written description set forth in the specification would not be considered to be sufficient by one of ordinary skill in the art to establish that Applicant was in possession of the claimed polypeptides.

As a first point, wherein the claims are drawn to a genus of "proteins comprising **an** amino acid sequence" encoded by the recited nucleic acid molecules, derivatives or fragments of said proteins, the claims are broadly but reasonably being interpreted as directed to a genus of structurally and functionally diverse proteins that need only comprise **an** amino acid sequence encoded by one of the recited nucleic acid molecules or be derivatives or fragments of said proteins. Notably, one of skill in the art readily appreciates that depending on the reading frame used in the recited nucleic acid molecule to translate the nucleic acid into an amino acid sequence and as well as

depending on where in the nucleic acid molecule sequence the translation was started that the recited nucleic acid molecules encode multiple structurally and functionally distinct polypeptides. Furthermore, the protein need only comprise **an** amino acid sequence encoded by such a nucleic acid and one of skill in the art readily appreciates that a protein comprising **an** amino acid sequence may merely comprise a fragment of the amino acid sequence encoded by the nuclei acid molecule as there are a plurality of amino acid sequences disclosed by the recited nucleic acid molecules. For example, one of skill in the art would consider every 2, 3, 4, 5, 6, etc., consecutive amino acid residues encoded by the recited nucleic acid molecules to be **an** amino acid sequence. Accordingly, because the polypeptides encompassed by this genus could have virtually any structure and function, it is apparent that these polypeptides do not share any particularly identifying (i.e., substantial) structural feature, which correlates with any one particularly identifying functional feature that is also shared by many, if not all, of these polypeptides which would allow one if skill in the art to immediately envision, recognize or distinguish as least most of its members from other proteins.

Notably, it is well-established in the art that there is a high degree of unpredictability in determining the three-dimensional structure and function of a given protein *a priori* given its amino acid sequence.

As evidenced by Jones (Pharmacogenomics Journal, 1:126-134, 2001), protein structure "prediction models are still not capable of producing accurate models in the vast majority of cases" (page 133, 3rd paragraph). Furthermore, Tosatto et al state, "the link between structure and function is still an open question and a matter of debate" (Current Pharmaceutical Design, 12:2067-2086, 2006, page 2075, 1st new paragraph). Therefore, even if the skilled artisan were able to submit a complete list of all the possible proteins, fragments and protein derivatives which fall within the scope of the claims, the skilled artisan would not be able to immediately envision, recognize or predict the three-dimensional structure and function of a given protein *a priori* based on this amino acid sequence.

Secondly, to address why the specification does not adequately describe the structurally and functionally diverse genera of proteins *comprising* the amino acid sequence of SEQ ID NO: 1 as set forth in claim 8, it is submitted that the specification fails to describe proteins *comprising* the amino acid sequence of SEQ ID NO: 1 as sharing any particularly identifying (i.e., substantial) structural feature, which correlates with any one particularly identifying functional feature that is also shared by members of this genus. In this case, the specification discloses the T128 polypeptide sequence of SEQ ID NO:1 which is 349 amino acids in length (see e.g., page 12 and Figure 1;yet does not identify any functional feature of a polypeptide with this amino acid sequence except that the T128 polypeptide antigen is highly expressed cancers, such as in prostate and gastric cancers (see e.g., page 2). However, it is apparent that the genus of polypeptides comprising the amino acid sequence of SEQ ID NO:1 in inclusive of structurally and functionally diverse polypeptides, because e.g., US 2003/0092616 A1 (Honda et al, 2003) teaches a different polypeptide which is 546 amino acids in length that comprises the amino acid sequence of SEQ ID NO:1[2] and WO 0058473 A2 (Shimkets et al, 2000) teaches another different polypeptide which is 401 amino acids in length that comprises the amino acid sequence of SEQ ID NO:1[3]. Once again, because there is a high degree of unpredictability in determining the function of a given protein based on its amino acid sequence alone, as evidenced by Jones and Tosatto et al (supra), one of skill in the art would not immediately envision or recognize that the polypeptides of US 2003/0092616 A1 and WO 0058473 A2 would function similarly to the polypeptide with the amino acid sequence of SEQ ID NO:1 instantly disclosed. For this reason, one of skill in the art would not recognize that the polypeptide with the amino acid sequence of SEQ ID NO:1 instantly disclosed was representative of the genus of polypeptides comprising the amino acid sequence of SEQ ID NO:1 and would not recognize that Applicant was in possession of the claimed genus. In this case, the specification fails to describe polypeptides comprising the amino acid sequence of SEQ

[2] See alignment attached as Exhibit A
[3] See alignment attached as Exhibit B

ID NO:1 as sharing any particularly identifying (i.e., substantial) structural feature, which correlates with any one particularly identifying functional feature that is also shared by those proteins.

Given the lack of particularity with which the proteins, fragments and derivatives to which the claims are directed, are described in the specification, it is submitted that the skilled artisan could not immediately envision, recognize or distinguish at least most of the members of these genera; and therefore the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

14. Claims 7-9, 26-28 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for making and using** an isolated polypeptide consisting of the amino acid sequence of SEQ ID NO:1, **and while being enabling for making and using** any polypeptides encompassed by the claims, which have been described by the prior art, **does not reasonably provide enablement for making and using** the claimed polypeptides comprising an amino acid sequence encoded by encoded by: a) a nucleic acid encoding SEQ ID NO: 1, a nucleic acid that encodes a polypeptide at least 80% identical to SEQ ID NO:1, or a fragment thereof, which is capable of cross-reacting with sera from patients with prostate cancer, b) nucleic acid molecules comprising the nucleotide sequence depicted between nucleic acid residues 642 b and 1688 of SEQ ID NO: 2, c) nucleic acid molecules which specifically hybridizes to said nucleic acid molecules, d) nucleic acid molecules the sequence of which differs from the sequence of said nucleic acid molecules due to the degeneracy of the genetic code, derivatives or fragments of said proteins or proteins comprising the amino acid sequence of SEQ ID NO:1. Furthermore, the specification **does not reasonably provide enablement for using the** claimed vaccine, immunogenic composition or kit for use with a method of detecting or monitoring cancer. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to enable the skilled artisan to use the claimed invention at the time the application was filed without undue experimentation.

MPEP § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

As set forth in the above rejection of the claims as lacking adequate written description, proteins comprising **an** amino acid sequence encoded by: a) a nucleic acid encoding SEQ ID NO: 1, a nucleic acid that encodes a polypeptide at least 80% identical to SEQ ID NO:1, or a fragment thereof, which is capable of cross-reacting with sera from patients with prostate cancer, b) nucleic acid molecules comprising the nucleotide sequence depicted between nucleic acid residues 642 b and 1688 of SEQ ID

NO: 2, c) nucleic acid molecules which specifically hybridizes to said nucleic acid molecules, d) nucleic acid molecules the sequence of which differs from the sequence of said nucleic acid molecules due to the degeneracy of the genetic code, derivatives or fragments of said proteins and proteins comprising the amino acid sequence of SEQ ID NO:1 are inclusive of polypeptides with widely divergent structures and functions. Accordingly, it is submitted that one of skill in the art would be subject to undue and unreasonable experimentation to make and use polypeptides commensurate in scope with the claimed invention, because the specification does not provide any specific, non-general guidance as to how to make such polypeptides, derivatives or fragments that are functionally equivalent to the polypeptide consisting of the amino acid sequence of SEQ ID NO:1 nor does the specification provide any specific, non-general guidance as to how to use these other polypeptides, derivatives or fragments with these widely divergent structures and functions as encompassed by the claims.

Once again, because it is well-established in the art that there is a high degree of unpredictability in determining the function of a given protein based on its amino acid sequence alone, as evidenced by Jones and Tosatto et al (supra), one of skill in the art would need specific guidance to enable them to make polypeptides, derivatives or fragments that are functionally equivalent to the polypeptide consisting of the amino acid sequence of SEQ ID NO:1.

In further support of this conclusion, Skolnick et al. (*Trends in Biotechnology* 2000; **18**: 34-39), for example, discloses that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (see, e.g., the abstract; and page 34, *Sequence-based approaches to function prediction*). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see, in particular, the abstract and Box 2).

In addition, Bowie et al. (*Science* 257: 1306-1310, 1990) teaches that an amino acid sequence encodes a message that determines the shape and function of a protein; and, that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome. Bowie et al. teaches that the determination of protein structure from sequence data and, in turn, utilizing structural determinations to ascertain functional aspects of the protein is extremely complex (page 1306, column 1).

For these reasons, it is evident that the skilled artisan cannot reliably predict without undue experimentation the functional properties of any given protein comprising **an** amino acid sequence of the recited nucleic acid molecules or the functional properties of any of the fragments or derivatives of these proteins and for this reason as well one of skill in the art would be subject to undue experimentation to make and use polypeptides, fragments and derivatives commensurate in scope with the claims.

Secondly, to further address the reasons that Applicant has not enabled the intended use of the claimed polypeptides in a vaccine or an immunogenic composition, it is submitted that the art recognizes that it is highly unpredictable whether a polypeptide can be used as a prophylactic vaccination to prevent cancer or as a vaccination to treat cancer based on immune responses, e.g., especially strategies drawn to immunizing patients against an established cancer, using, for example any cancer vaccine or an immunogenic composition. Notably, while the specification teaches that the polypeptides of the invention can be used in vaccines or immunogenic compositions for the prophylactic prevention of cancer or the treatment of cancer, at e.g., page 11, the specification lacks any specific, non-general guidance that would enable one of skill in the art to use the claimed vaccines of immunogenic compositions in this manner. For example, DeGruijl T. D. et al (Nature Medicine, 5(10): 1124-1125, Oct. 1999) state that a variety of anti-tumor vaccine trials have been undertaken and in spite of the large number of these trials, and the plethora of distinct approaches investigated, there has been little evidence of clinical efficacy. DeGruijl also states

"precise correlates of clinical effects and immunological responses have been lacking" (see page 1124, left column).

To further elaborate on the unpredictability of using cancer vaccines or immunogenic compositions to prevent or treat cancer, Wang et al. (*Exp. Opin. Biol. Ther.* 2001; **1** (2): 277-290) teaches the "melanoma model" is the paradigm for studies of the effectiveness of cancer vaccines; see entire document (e.g., the abstract). Wang et al. teaches, "the success of these approaches has been limited [save for scattered reports] and T-cell-directed vaccination against cancer remains at a paradoxical standstill whereby anticancer immunisation can be induced but it is not sufficient, in most cases, to induce tumour regression" (abstract). In order to explain the lack of clinical success, despite the promise of preclinical data, Wang et al. teaches, among other reasons, clinical data suggest the possibility of a dissociation between immune responses detected in peripheral blood *versus* tumor, which suggests that is more important to determine immune response at the tumor site, rather than in the peripheral blood, in assessing the likely effectiveness of the treatment (page 281, column 1). Regardless of the cause for such poor extrapolation of preclinical findings, Wang et al. discloses the difficulty of correlating laboratory findings with clinical outcome is a significant obstacle to the assessment of the role of immune escape and/or tolerance in cancer progression (page 282, column 2). Furthermore, Wang et al. teaches, "[t]he published experience using the ELISPOT [assay] to monitor T-cell responses to cancer antigens is still limited" (page 283, column 2); and Wang et al. teaches the same is true of the "tetramer" assay (page 284, column 2). Wang et al. teaches, "there are no universally accepted correlates at this time between any method of in vitro immune monitoring and clinical outcome" (page 285, column 1).

Thus, due in part to the inadequacy of the methods used to assess the immune response mustered upon vaccination and the poor correlation of such results and clinically relevant endpoints, such as tumor regression, the art of cancer immunotherapy is highly unpredictable. Bodey et al. (*Anticancer Research.* 2000; **20**: 2665-2676) teaches, "while cancer vaccine trials have yielded tantalizing results, active

immunotherapy has not yet become an established modality of anticancer therapy" (page 2665, column 2). As to the current state of the art, Bodey et al. comments, "the use of active specific immunotherapy (ASI) for cancer (cancer 'vaccines') is still in its scientific infancy despite several decades of clinical and basic research" (page 2668, column 2). Thus, little has changed to alter the artisans' expectations of the still prospective vaccine immunotherapy field. Cox et al. (*Science.* 1994; **264**: 716-719) teaches, "neither adoptive transfer of melanoma-specific CTLs nor specific active immunotherapy with whole melanoma cells or cell-derived preparations has led to the eradication of melanoma in more than a minority of patients" (page 716, column 2). Then again, even that small note of promise has since faded. Bodey et al. discloses, "ASI in at least one instance may have cured melanoma in a patient with metastatic disease, but that patient developed another immunologically and genetically distinct melanoma" (page 2668, column 2). In the abstract Bodey et al. speculates upon the reasons that ASI is ineffective or lacks efficacy:

> The theoretical basis for all of these approaches is very well founded. Animal models, albeit highly artificial, have yielded promising results. Clinical trials in humans, however, have been somewhat disappointing. Although general immune activation directed against the target antigens contained with a cancer vaccine has been documented in most cases, reduction in tumor load has not been frequently observed, and tumor progression and metastasis usually ensue, possibly following a slightly extended period of remission. The failure of cancer vaccines to fulfill their promise is due to the very relationship between host and tumor: through a natural selection process the host leads to the selective enrichment of clones of highly aggressive neoplastically transformed cells, which apparently are so dedifferentiated that they no longer express cancer cell specific molecules. Specific activation of the immune system in such cases only leads to lysis of the remaining cells expressing the particular TAAs [tumor associated antigens] in the context of the particular human leukocyte antigen (HLA) subclass and the necessary costimulatory molecules. The most dangerous clones of tumor cells however lack these features and thus the cancer vaccine is of little use.

Furthermore, Boon (*Advances in Cancer Research*. 1992; **58**: 177-210) teaches that for successful application of active immunization in human patients, we have to stimulate immune defenses of organisms that have often carried a large tumor burden. Establishment of immune tolerance may therefore have already occurred in the patient and in such cases, active specific immunization will be fruitless, since anergic CTL cannot be activated, will not proliferate, and are deficient in effector function. Several

lines of evidence suggest that large tumor burdens can tolerize, or at least depress the capability to respond against the tumor (page 206, paragraph 2). Furthermore, among other mechanisms, Arceci (*Journal of Molecular Medicine.* 1998; **76**: 80-93) teaches, "it has been hypothesized that tumor cells may escape immune recognition and subsequent killing by failing to satisfy one or more of the [...] requirements for T cell antigen recognition and activation. For example, if antigen presentation does not occur because of low or absent expression of MHC or lack of a recognizable tumor antigen, then tumor cells would not be recognized" (page 83, column 2). Areci continues, "on the other hand, if antigen recognition occurs by T cells but tumor cells do not express a costimulatory molecule, then T cells might become anergic to the tumor cells" (page 83, column 2). Notably, Areci teaches, "most solid tumors usually do not express costimulatory molecules" (page 84, column 1).

In this case, the specification does not present sufficient evidence or nexus that would enable the skilled artisan to induce tumor immunity or treat cancer by inoculating an individual with a vaccine or immunogenic composition comprising the claimed polypeptides and for these reasons, one of skill in the art would be subject to undue and unreasonable experimentation to use the claimed vaccines and immunogenic compositions.

In view of the lack of the predictability of the art to which the invention pertains, the lack of established clinical protocols for effective cancer vaccine therapies, undue experimentation would be required to practice the claimed vaccine or immunogenic composition. Absent a specific and detailed description in applicant's specification of how to effectively practice the claimed vaccine and absent working examples providing evidence which is reasonably predictive that the claimed vaccine is effective for vaccinating individuals against cancer, commensurate in scope with the claimed invention, one of skill in the art would be subject to undue experimentation without reasonable expectation of success to use the claimed polypeptides in a vaccine or immunogenic composition.

Finally, while the specification discloses at page 9 that the invention includes, "[k]its for detecting or monitoring cancer, such as gastro-intestinal cancer, including gastric cancer and/or colorectal cancer, or prostate cancer, using polypeptides, nucleic acids or antibodies according to the invention are also provided. Such kits may additionally contain instructions and reagents to carry out the detection or monitoring", the specification lacks any specific, non-general guidance that would enable one of skill in the art to use the claimed polypeptides with methods of detecting or monitoring cancer.

Notably, methods of detecting or monitoring cancer are broadly, but reasonably interpreted to include methods of diagnosing cancer, methods of prognosing cancer, methods of predicting the development of cancer, methods of predicting which treatments will be effective in an individual with cancer and/or any other methods wherein cancer is somehow "detected" or "monitored". However, it is well-established in the art that even methods of diagnosis of cancer are highly unpredictable in the art because one of skill in the art readily appreciates that measuring tumor marker levels alone is insufficient to provide a diagnosis of cancer. For example, the National Cancer Institute (Cancer Facts, Fact Sheet 5.18, 1998) teaches that measurements of tumor marker levels need to be coupled to other clinical tests for the detection and diagnosis of cancer (see entire document, e.g., page 1, 2nd paragraph). Notably, this fact sheet explicitly states the following:

> "measurements of tumor marker levels alone are **not** sufficient to diagnose cancer for the following reasons:
>
> • Tumor marker levels can be elevated in people with benign conditions.
>
> • Tumor marker levels are not elevated in every person with cancer---especially in the early stages of the disease.
>
> • Many tumor markers are not specific to a particular type of cancer; the level of a tumor marker can be raised by more than one type of cancer."

Therefore, one of skill in the art would be subject to undue experimentation to use the claimed kits for their recited intended use with a method of detecting or

monitoring cancer because the specification does not teach any methods of detecting or monitoring cancer that use any of the claimed polypeptides.

Applicant is reminded that reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

In deciding *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970), the Court indicated the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. "Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 1001, 1005 (CA FC 1997).

In conclusion, upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the amount of guidance, direction, and exemplification disclosed in the specification, as filed, is not deemed sufficient to have enable the skilled artisan to make and/or use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 7, 9, 26, 27, 28 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 6,348,579 (Hodgson, 2002).

The claims are herein drawn to an isolated protein comprising an amino acid sequence encoded by nucleic acid molecules encoding SEQ ID NO:1 or a derivative of said protein. Notably, because an amino acid sequence would broadly, but reasonably be interpreted to include any two consecutive amino acids encoded by nucleic acid molecules encoding SEQ ID NO:1, any polypeptide that comprises two consecutive amino acids in common with SEQ ID NO:1 is a protein comprising an amino acid sequence encoded by nucleic acid molecules encoding SEQ ID NO:1 Furthermore, while claims 26, 28 and 31 recite a vaccine comprising said protein and a pharmaceutically acceptable carrier, a kit comprising said protein for use with a method of detecting or monitoring cancer, or an immunogenic composition comprising said protein and a pharmaceutically acceptable carrier, respectively, these recitations are interpreted as an intended use of a composition comprising said protein and a pharmaceutically acceptable carrier because these recitations do not materially and/or structurally define the claimed product.

In this case, the specification does not expressly define the phrases “vaccine”, “kit” or “immunogenic composition” as comprising any particular structure and therefore, it is submitted that these recitations do not materially and/or structurally distinguish a composition comprising said protein from a “vaccine”, “kit” or “immunogenic composition” comprising said protein.

Claim 27 is further drawn to said protein attached to a carrier protein. In this case, the specification does not expressly define the phrase “carrier protein”, and therefore, this phrase is broadly, but reasonably interpreted to include attachment of any other amino acid sequence to said protein.

US Patent 6,348,579 teach an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:2 (see entire document, e.g., claim 1 and SEQ ID NO:2). This protein comprises an amino acid sequence “EE” at amino acids 63 and 64 which is the same as an amino acid sequence encoded by nucleic acid molecules encoding SEQ ID NO:1, see e.g., amino acids 52 and 53 of SEQ ID NO:1 which are “EE”. US Patent 6,348,579 further teaches said protein in compositions comprising pharmaceutically

acceptable carriers, such as water and said protein fused to a heterologous amino acid sequence, which, absent a showing of any difference, is being considered a "derivative" of said protein and said protein "attached to a carrier protein" (see, e.g., column 20 and claims 2-6).

Accordingly, US Patent 6,348,579 teaches proteins and compositions which are materially and structurally indistinguishable from the claimed proteins and compositions. Therefore, absent a showing of any difference, the claimed proteins and compositions and the proteins and compositions disclosed by the prior art are deemed the same and US Patent 6,348,579 anticipates the claimed invention.

17. Claims 7-9, 26, 27, 28 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent Application Publication No. 2003/0092616 A1 (Matsuda et al, 2003).

The claims are herein drawn to an isolated protein comprising the amino acid sequence of SEQ ID NO:1 or a derivative of said protein and, for the reasons explained in the above 102(b) rejection, compositions comprising said protein and a pharmaceutically acceptable carrier, such as water.

Claim 27 is further drawn to said protein attached to a carrier protein. In this case, the specification does not expressly define the phrase “carrier protein”, and therefore, this phrase is broadly, but reasonably interpreted to include attachment of any other amino acid sequence to said protein.

US 20030092616 A1 teaches an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:74 (see entire document, e.g., pages 2 and 4 and SEQ ID NO:74). This protein comprises the instantly claimed SEQ ID NO:1 (see alignment attached as Exhibit A) attached to a 197 amino acid sequence at the N-terminus. US 20030092616 A1 further teaches said protein fused to other amino acid sequences, which, absent a showing of any difference, is being considered a "derivative" of said protein and said protein "attached to a carrier protein" (see e.g., page 12). Finally, US

20030092616 A1 teaches said polypeptide in compositions comprising water, i.e., a pharmaceutically acceptable carrier. (see, e.g., pages 5 and 15).

Accordingly US 20030092616 A1 teaches proteins and compositions which are materially and structurally indistinguishable from the claimed proteins and compositions. Therefore, absent a showing of any difference, the claimed proteins and compositions and the proteins and compositions disclosed by the prior art are deemed the same and US 20030092616 A1 anticipates the claimed invention.

18. Claims 7-9, 26, 27, 28 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/58473 A2 (Shimkets et al, 2000).

The claims are herein drawn to an isolated protein comprising the amino acid sequence of SEQ ID NO:1 or a derivative of said protein and, for the reasons explained in the above 102(b) rejection, compositions comprising said protein and a pharmaceutically acceptable carrier, such as water.

Claim 27 is further drawn to said protein attached to a carrier protein. In this case, the specification does not expressly define the phrase “carrier protein”, and therefore, this phrase is broadly, but reasonably interpreted to include attachment of any other amino acid sequence to said protein.

WO 00/58473 A2 teach an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:4798 (see entire document, e.g., pages 2 and SEQ ID NO:4798). This protein comprises the instantly claimed SEQ ID NO:1 (see alignment attached as Exhibit B) attached to a 52 amino acid sequence at the N-terminus. WO 00/58473 A2 further teaches said protein fused to other amino acid sequences, which, absent a showing of any difference, is being considered a "derivative" of said protein and said protein "attached to a carrier protein" (see e.g., page 31). Finally, WO 00/58473 A2 teaches said polypeptide in compositions comprising a pharmaceutically acceptable carrier. (see, e.g., page 2).

Accordingly WO 00/58473 A2 teaches proteins and compositions which are materially and structurally indistinguishable from the claimed proteins and compositions.

Therefore, absent a showing of any difference, the claimed proteins and compositions and the proteins and compositions disclosed by the prior art are deemed the same and WO 00/58473 A2 anticipates the claimed invention.

Double Patenting

19. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

20. Claims 7, 9, 26, 27, 28 and 31 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 8-10 of copending Application No. 10/569,572. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons:

The instant claims are described supra.

Claims 8-10 of copending Application No. 10/569,572 are drawn to an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:3 and derivatives thereof. This protein comprises an amino acid sequence "EE" which is the same as an amino acid sequence encoded by nucleic acid molecules encoding SEQ ID NO:1, see

e.g., amino acids 52 and 53 of SEQ ID NO:1 which are "EE". Furthermore, while copending Application No. 10/569,572 does not expressly claim compositions or said protein further attached to a carrier protein, it is submitted that such compositions and fusion proteins would be obvious variants of Claims 8-10 of copending Application No. 10/569,572 because to produce an isolated protein, the protein is necessarily in an aqueous composition comprising water, and because one of skill in the art would immediately envision attaching a carrier protein to such a protein to facilitate recombinant expression and purification of such a protein.

Accordingly, the claimed inventions are so substantially similar that for the most part, the claimed subject matter of the copending application anticipates the claimed subject matter of the instant application and any minor differences in the subject matter claimed in the instant application would be seen as an obvious variation of the subject matter claimed in the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

21. No claims are allowed.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brad Duffy whose telephone number is (571) 272-9935. The examiner can normally be reached on Monday through Friday 7:00 AM to 4:30 PM, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully,
Brad Duffy
571-272-9935

/Stephen L. Rawlings/
Primary Examiner, Art Unit 1643

/bd/
Examiner, Art Unit 1643
June 7, 2008